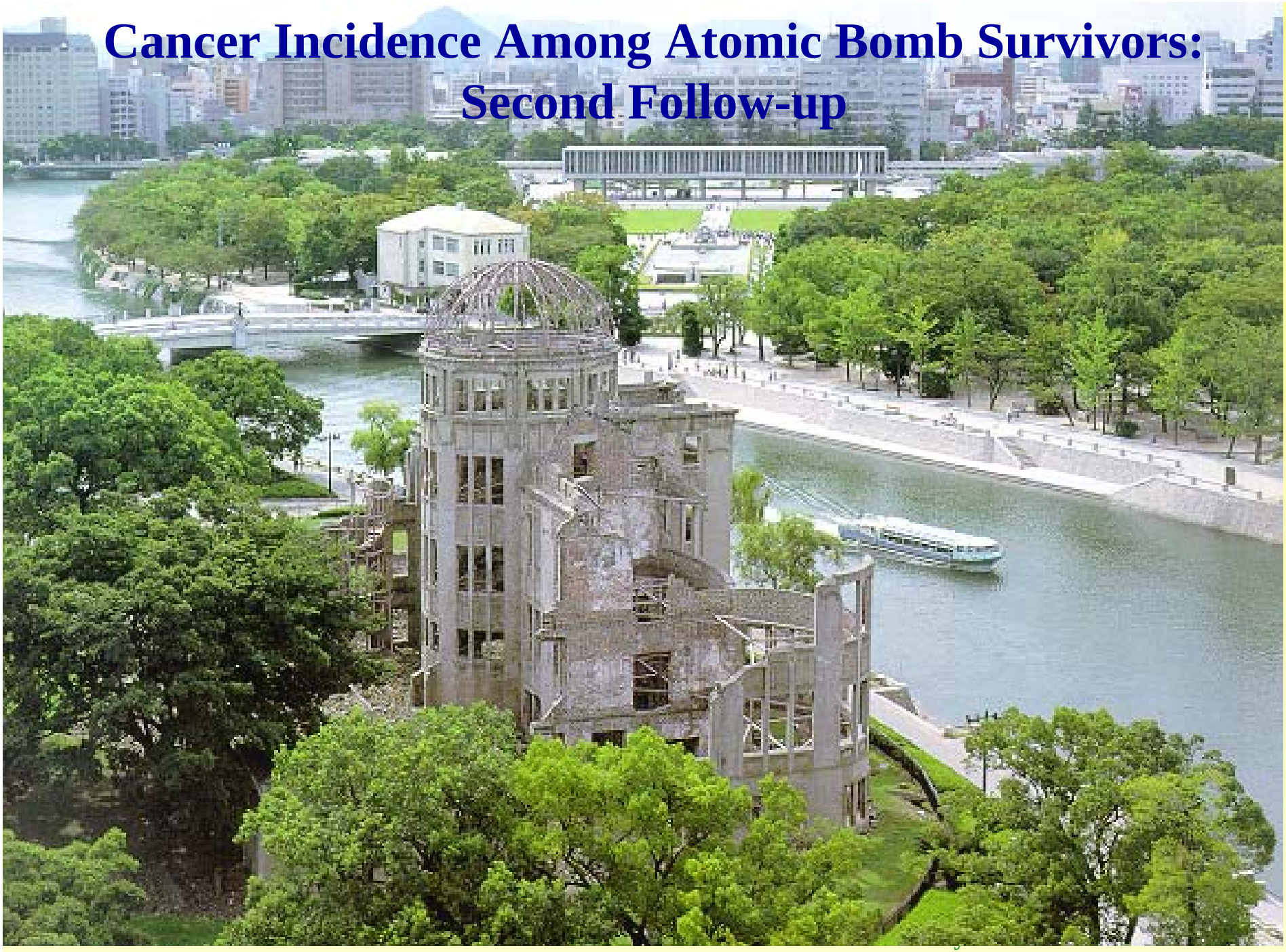
Cancer Incidence Among Atomic Bomb Survivors: Second Follow-up



Outline

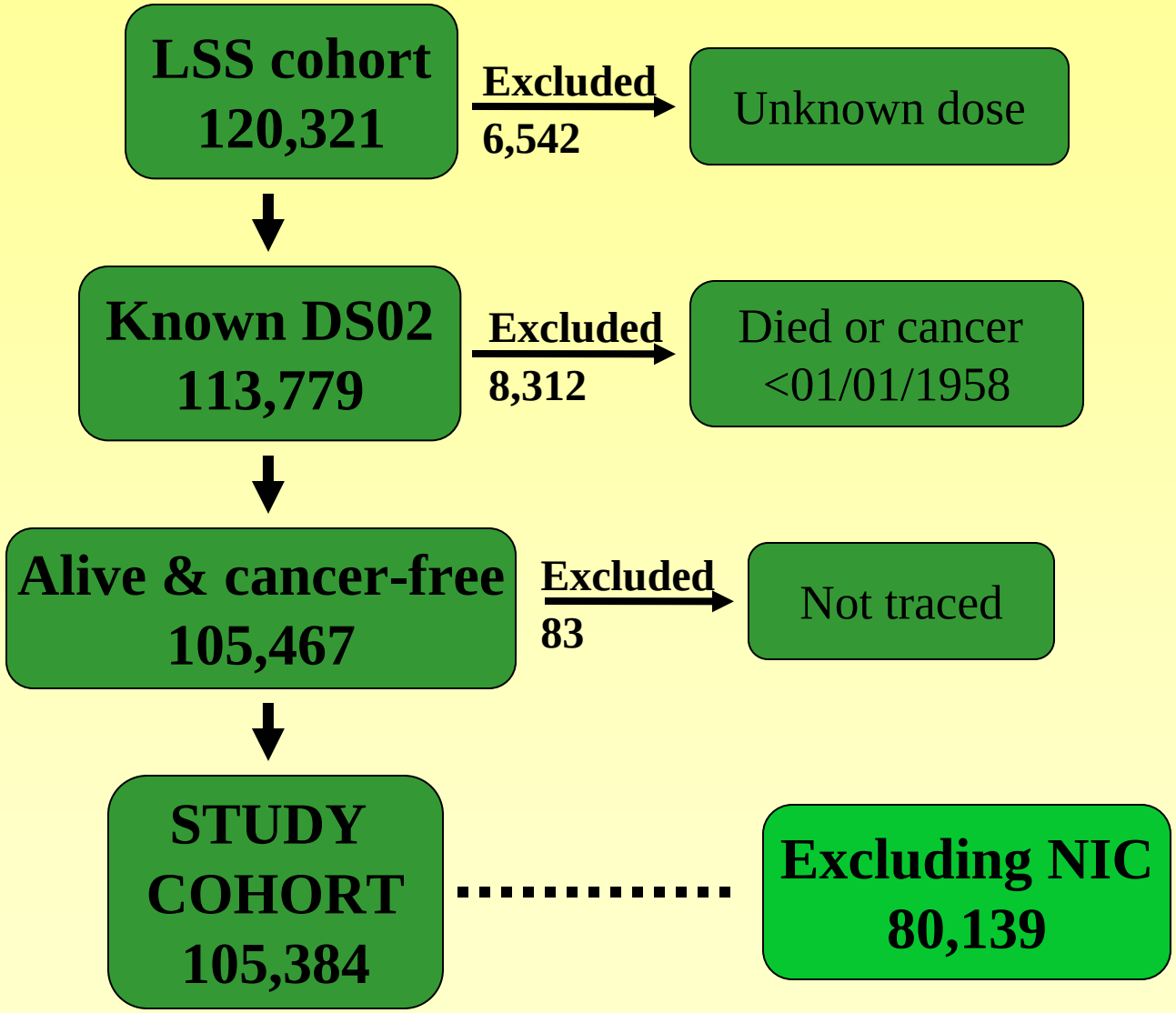
- Life Span Study (LSS) cancer incidence cohort
- Cancer incidence follow-up 1958-1995
- Major results
  - All solid cancers
  - Site-specific risks
- Summary remarks

Objectives of Incidence Report

- Quantify cancer risks attributable to radiation
- Explore the shape of the dose-response
- Assess how the risk is modified by age, time, gender and other factors
- Seek insights into site-specific differences in risk patterns

LSS Cancer Incidence Cohort

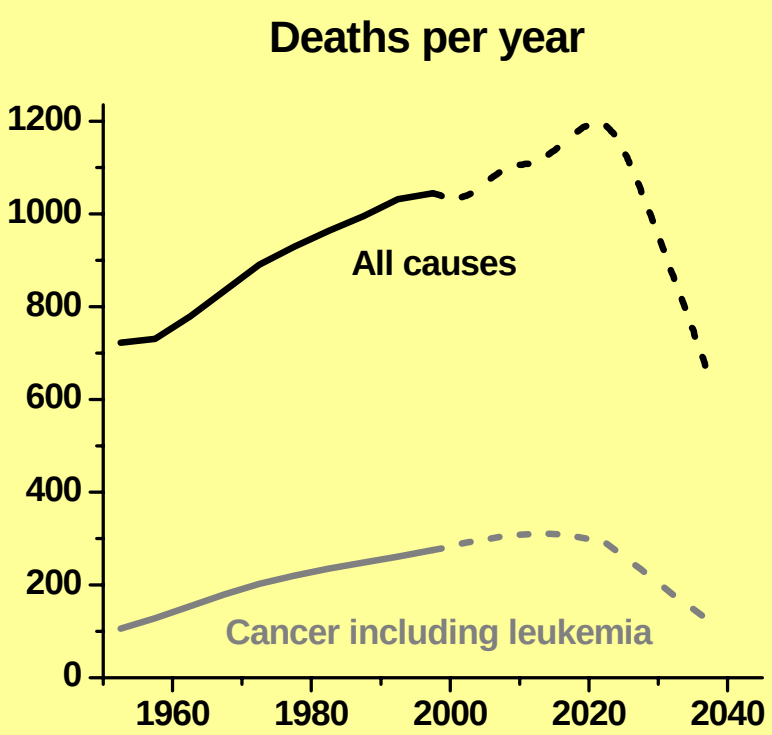
- Survivors within 2.5 km of the bombings
- Survivors within 2.5 -10 km
- Not-in-city (NIC)
- Known DS02 dose
- Alive and cancer free in 1958

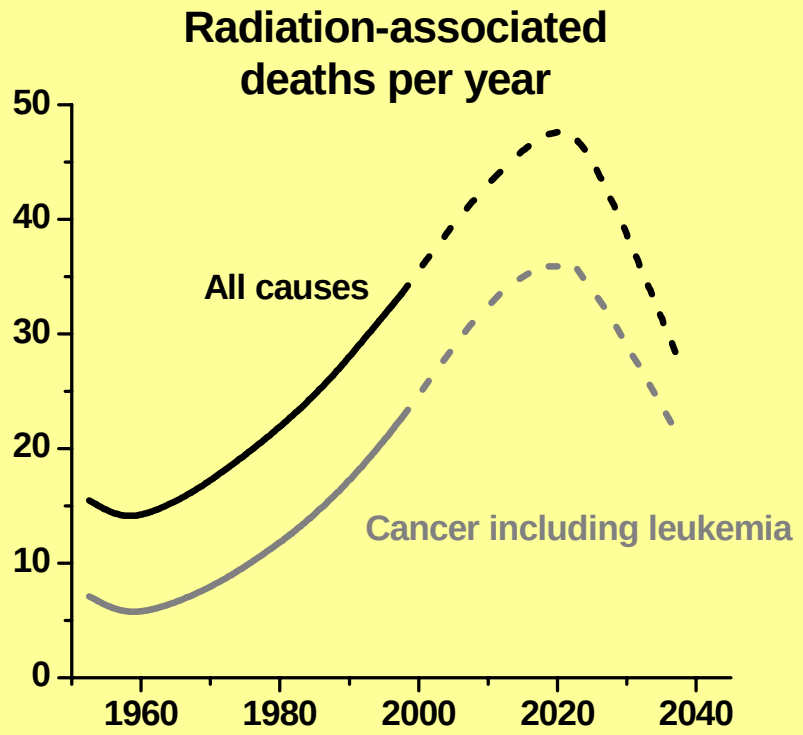


Strengths of LSS Incidence Cohort

- Large study population
- Basically healthy non-selected population
- All ages and both sexes
- Well characterized dose estimates
- Wide range of doses
- Complete ascertainment in tumor registry catchment areas
- More than 50 years of follow-up

Projections:
Aging of Younger Cohorts





Updated Cancer Incidence Report

- 1958-1998
- 105,384 people
- 44% alive in 2000
  - ~85% of those <20 at the time of the bombings
- First primary tumors
- DS02 organ dose estimates

LSS Cohorts

	Incidence	Mortality
Yr. follow-up began	1958	1950
Study population*	80,139	86,572
Mean age at bomb	26.8	29.0
Endpoint	Cancer only	All deaths
Ascertainment	Cancer registries	Family registry
Catchment area	Hiroshima and Nagasaki	All Japan

** Excluding NIC*

Strengths of LSS Cancer Incidence Data

- Data on non-fatal cancers
- High level cancer ascertainment
- Accurate diagnoses
- Information on histology
- Includes some benign tumors
- Long follow-up

LSS Tumor Registry

Hiroshima & Nagasaki catchment area

Active case ascertainment

- *Large hospitals*
- *Tissue registries*
- *Death certificates*
- *Medical associations (small hospitals)*

No dose bias in case ascertainment

Limitations of LSS Cancer Incidence Data

- No solid cancer data from 1945-1958
- No leukemia data from 1945-1950
- Cancer data limited to Hiroshima and Nagasaki area residents
- Limited treatment data

LSS COHORT

Dose, Sv	Subjects	(%)
< 0.005	34,582	43.2
0.005 - 0.1	29,352	36.6
0.1 - 0.2	5,316	6.6
0.2 - 0.5	5,897	7.4
0.5 - 1	3,057	3.8
1 - 2	1,503	1.9
2+	436	0.5

Magnitude of Doses

A-bomb survivors: Average dose ~ 0.25 Sv

Nuclear workers: Average dose ~0.004 Sv/yr

Environmental exposure: Doses < 0.001 Sv

Diagnostic medical exposures: 0.001-0.01 Sv*

Therapeutic medical exposures: Can be as high as 80 Sv

**** Lower doses for x-rays higher for CT***

Statistical Methods

- DS86 total kerma (>4 Gy = 4 Gy)
- Tumor registry catchment area
- Migration adjustment of person years
- General excess relative (ERR) and absolute (EAR) risk models
- Linear dose-response standard model
- Modifying effects of gender and age

LSS Cancer Incidence Data

Period	Person Years*	Cases
1958-1995^	1,989,123	12,161
1958 – 1987	1,655,000	8,613

**Adjusted for migration from catchment area*

^ Does not includes NIC

Preliminary data – not for distribution

Distribution of Solid Cancers

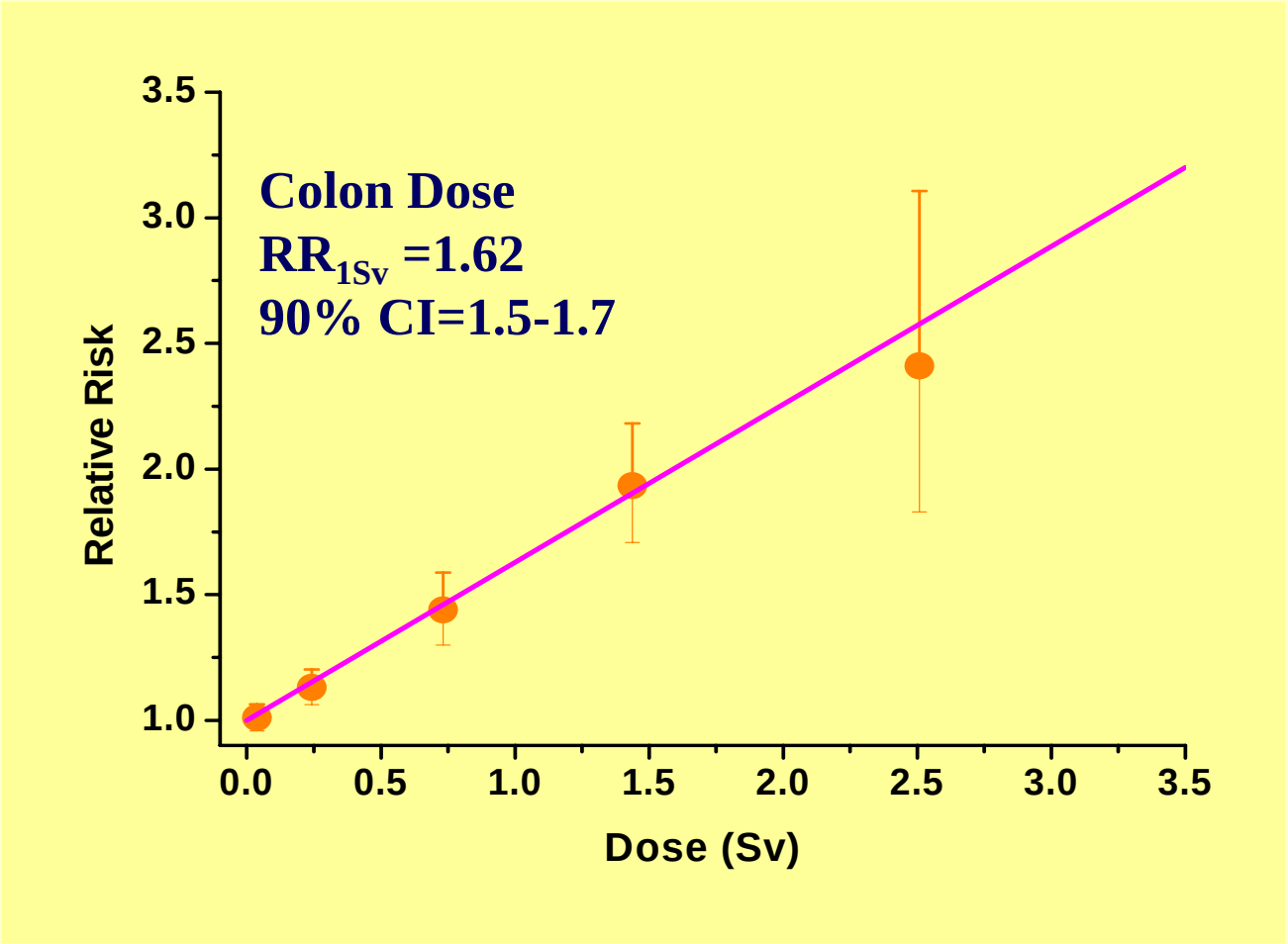
Site	1958-87	1958-95
Digestive system	4,797	6,893
Respiratory system	1,027	1,413
Female genital	891	1,062
Breast	529	777
Urinary system	325	501
Thyroid	225	384
Skin	181	260
Male genital	160	266
Oral cavity	132	180
Nervous system	125	183

Solid Cancers: 1958 - 1995

Dose, Sv	Observed	RR	Excess
< 0.005	4,901	1.00	1
0.005 - 0.1	4,184	1.01	77
0.1 - 0.2	883	1.11	68
0.2 - 0.5	1,044	1.20	169
0.5 - 1	626	1.45	188
1-2	392	1.94	174
2+	116	2.42	80

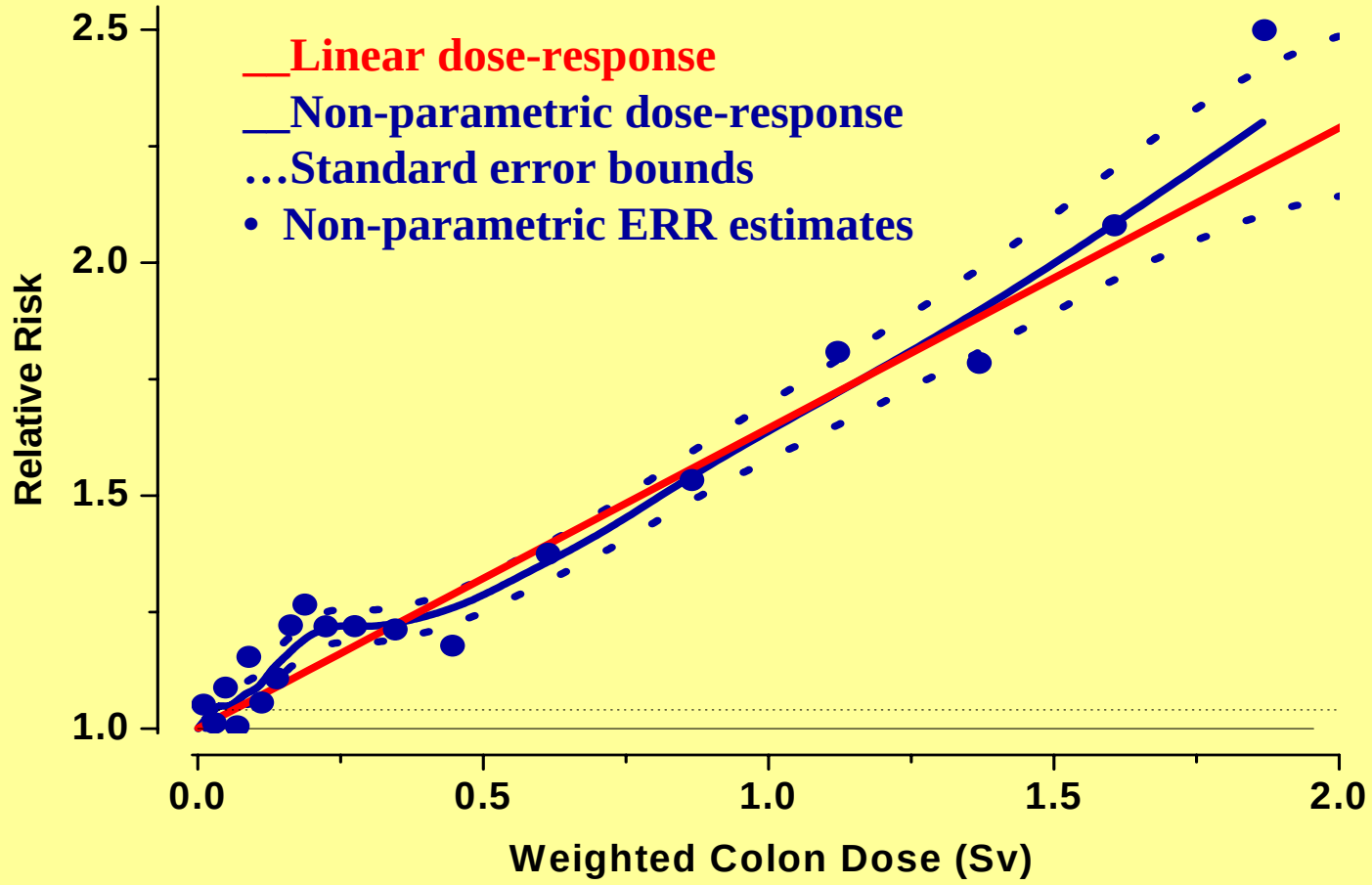
757 excess cancers

Solid Cancers



Preliminary data – not for distribution

Solid Cancer Incidence Dose Response



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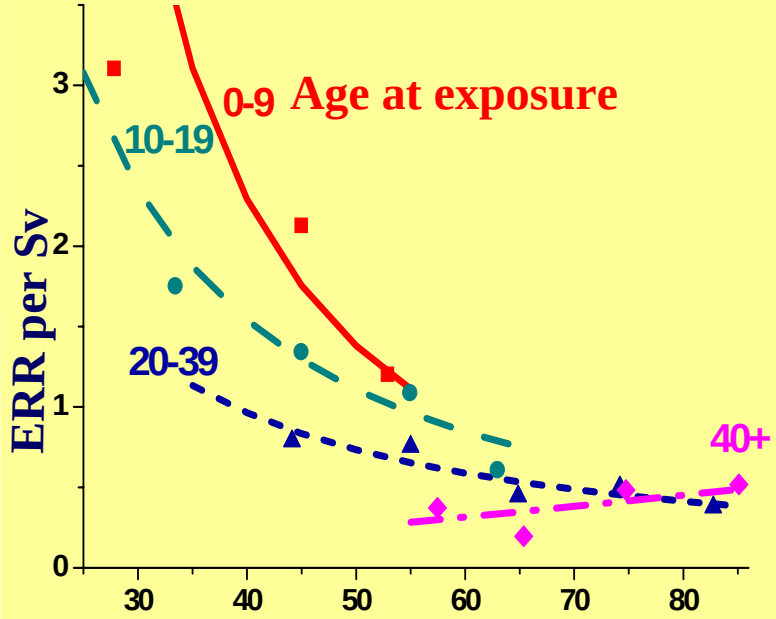
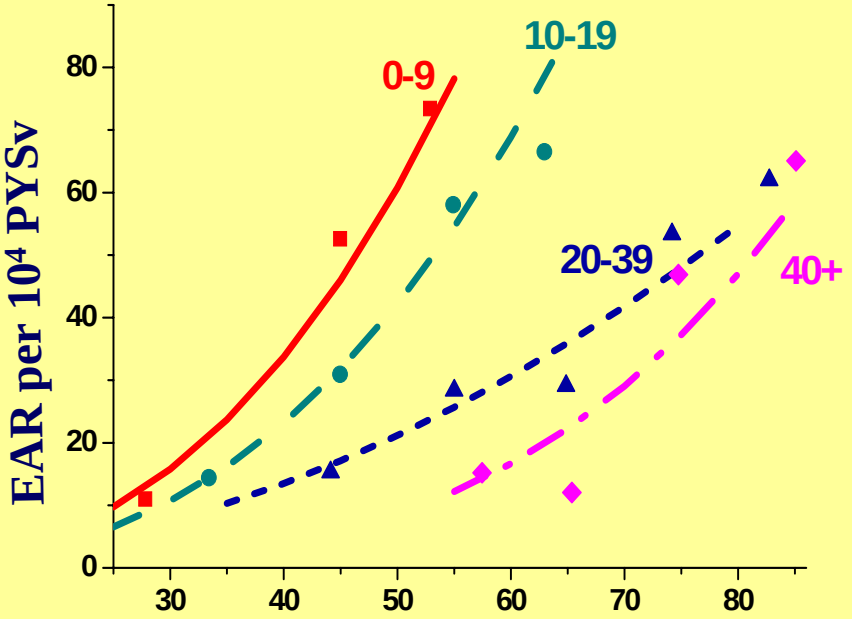
Solid Cancer Temporal Patterns

Excess Relative Risk



Excess Absolute Rate

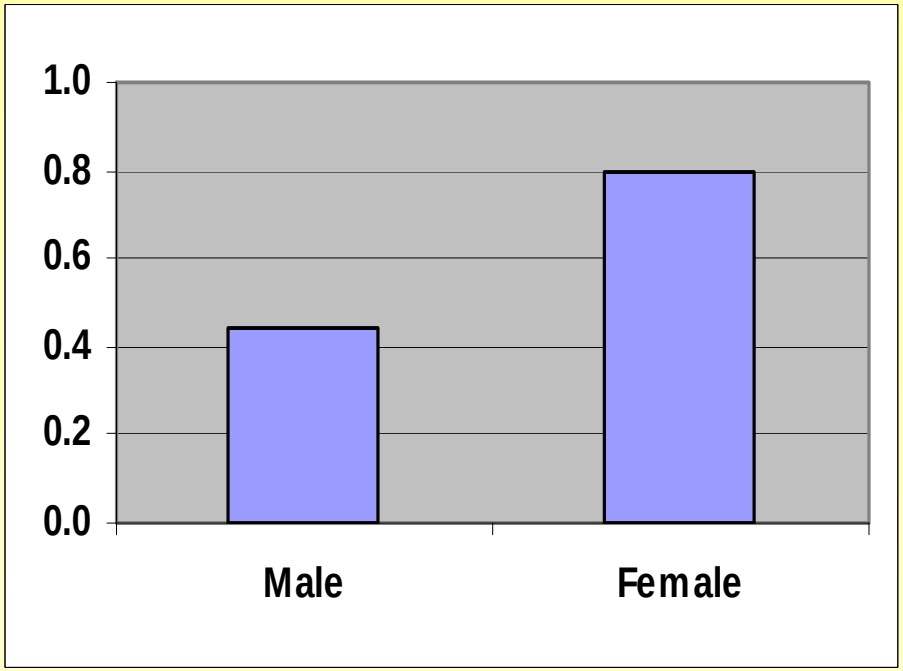


Attained Age

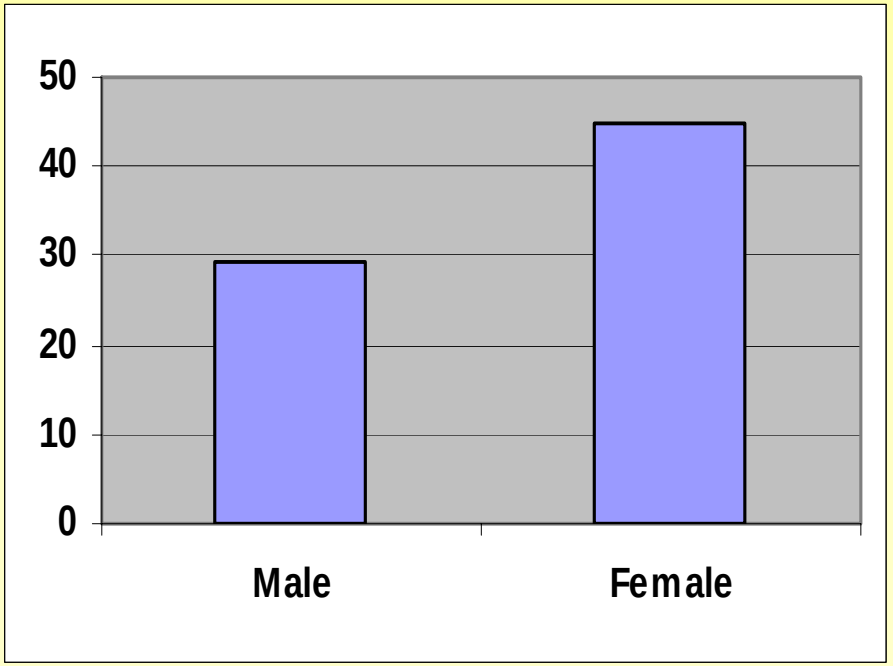
Preliminary data – not for distribution

Solid Cancer Risks by Gender
(for person age 60 exposed at age 30)

ERR per Sv



EAR per 10,000 PY Sv

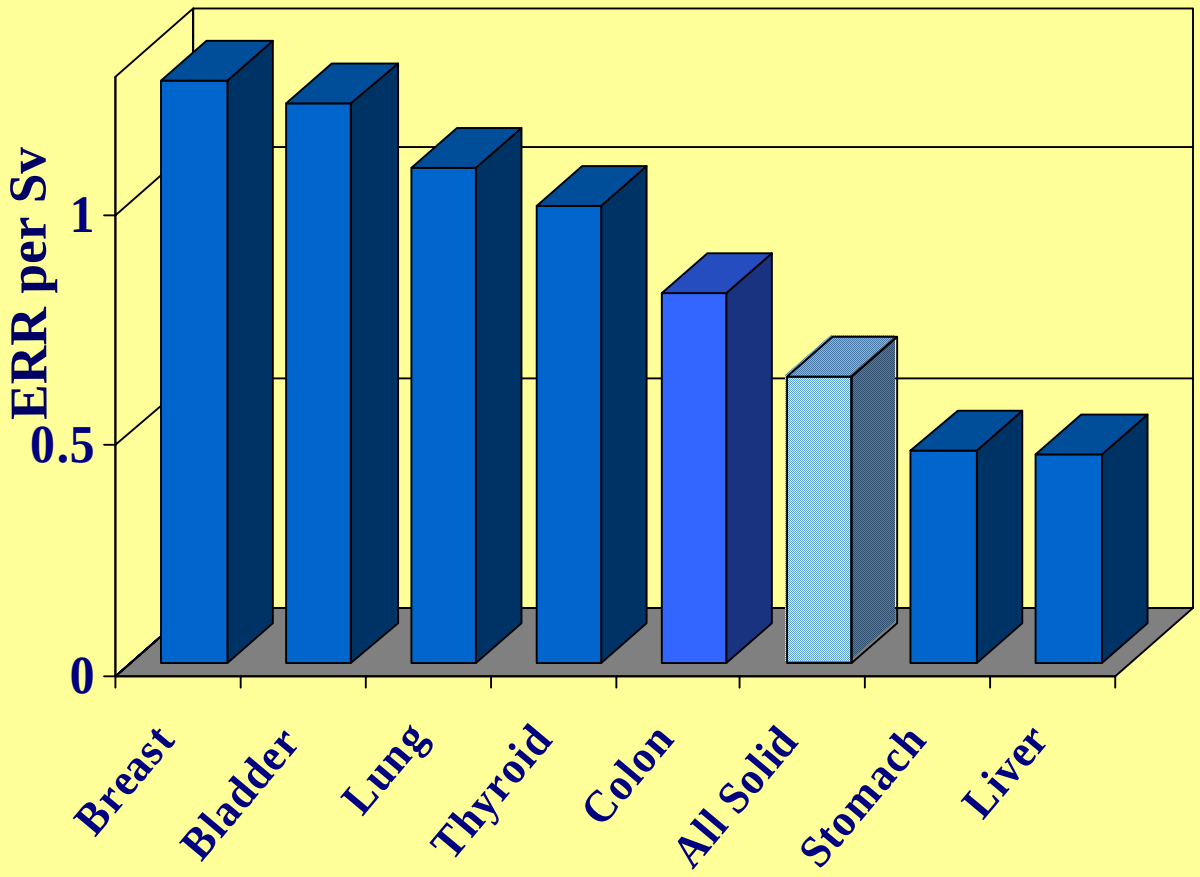


Preliminary data – not for distribution

Site–Specific Risks

Site–Specific Risk Estimates

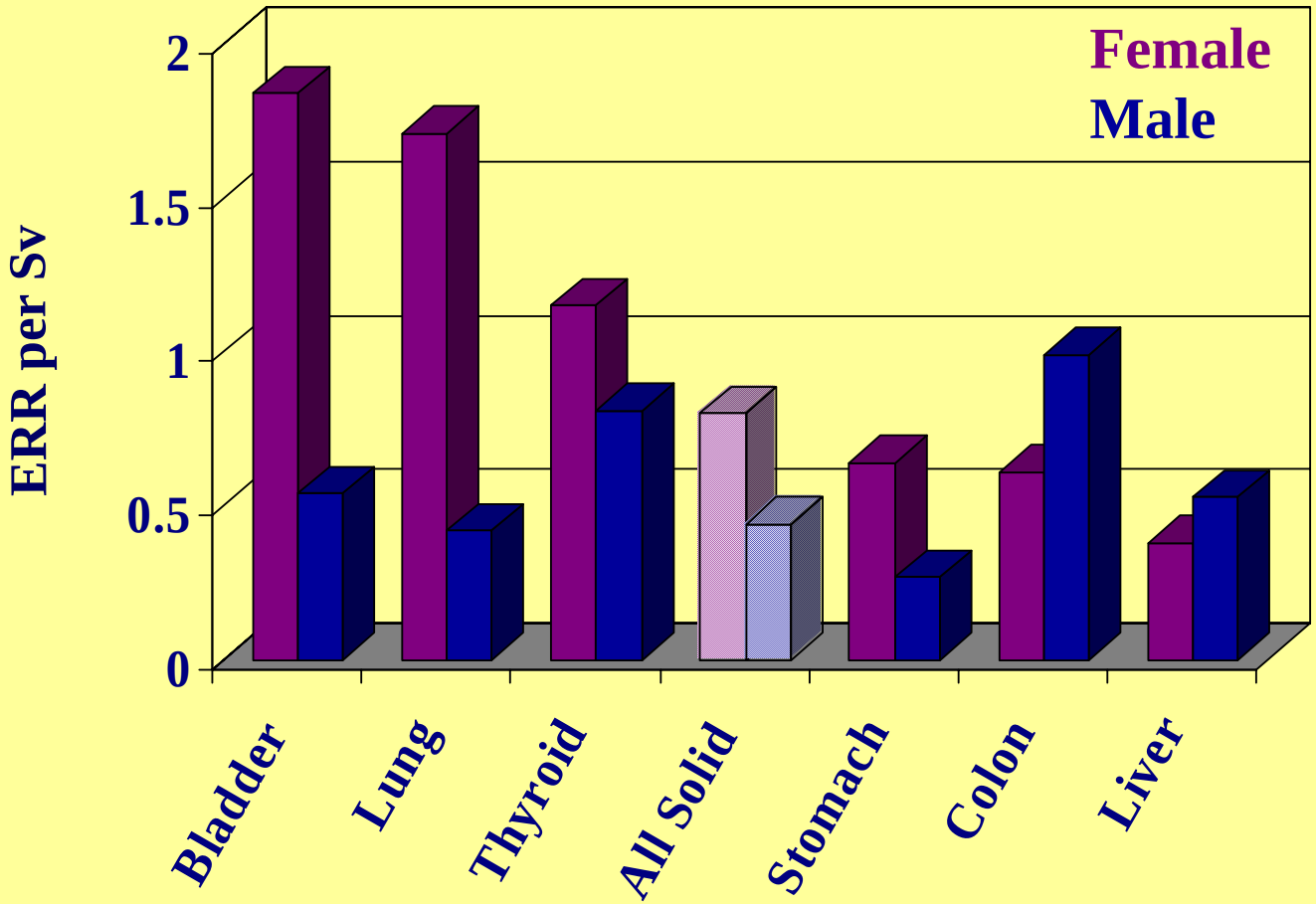
(for person age 60 exposed at age 30)



Preliminary data – not for distribution

Gender Effects

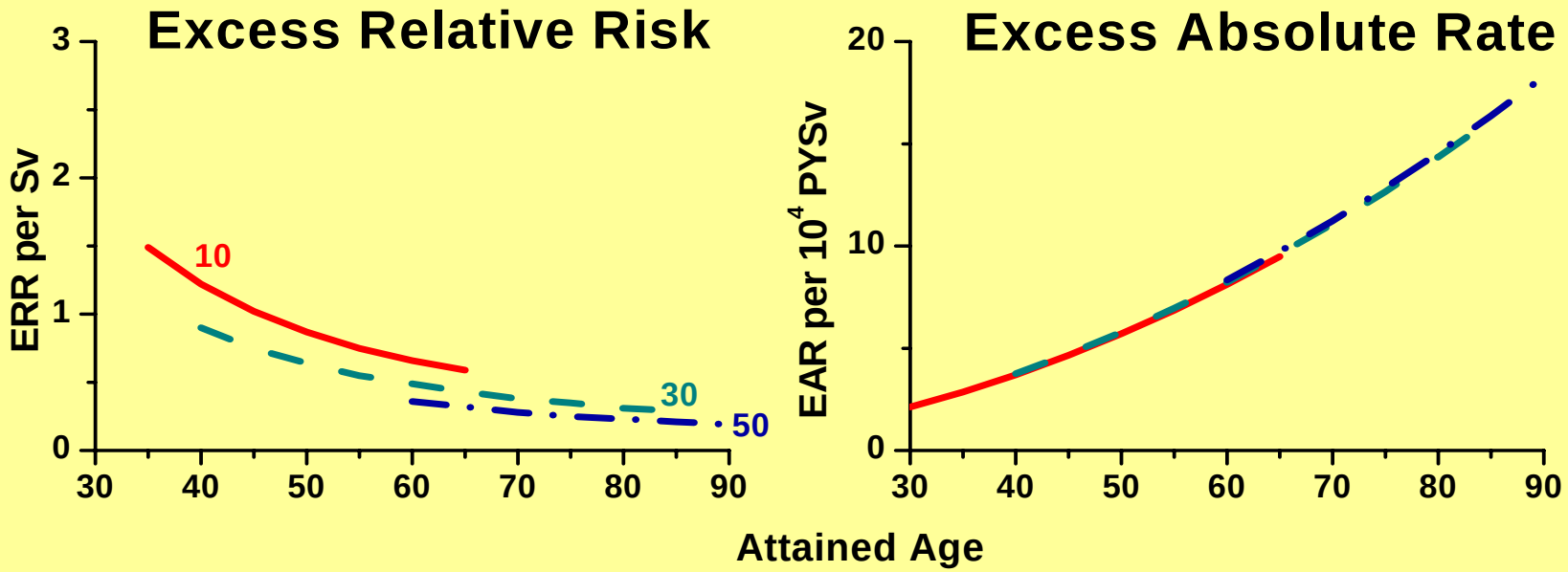
(for person age 60 exposed at age 30)



Preliminary data – not for distribution

Stomach Cancer

142 excess cases among 3,354



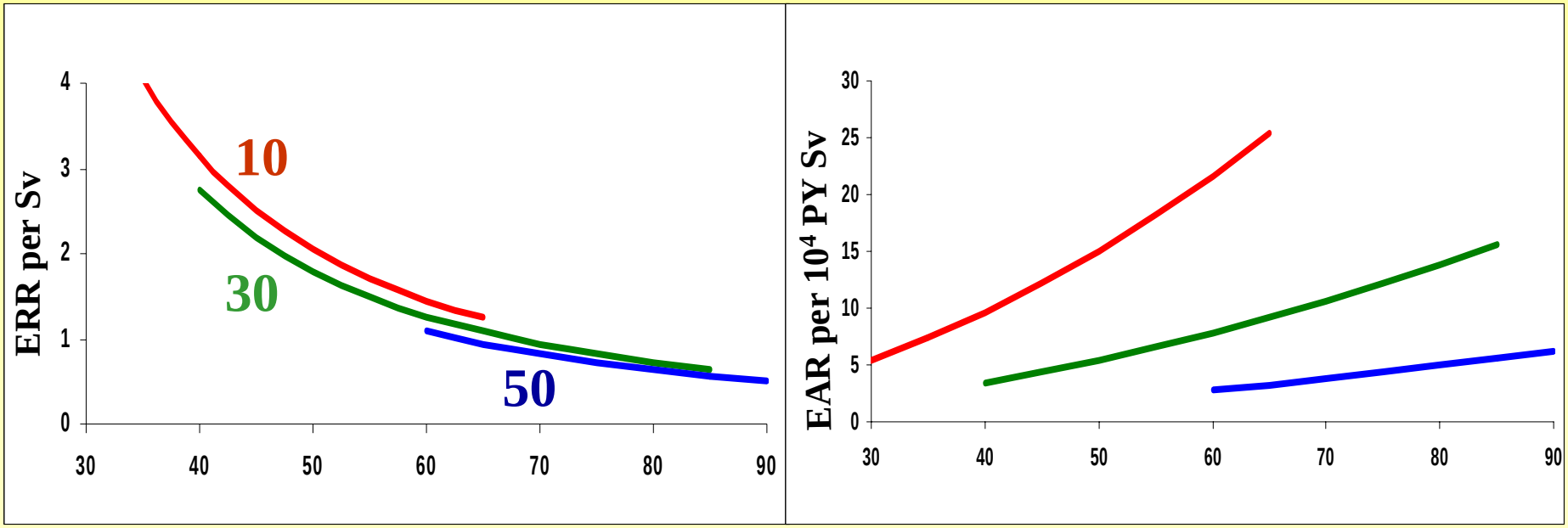
ERR/Sv = 0.46* **EAR/10^4 PYSv = 7.7***

***for person age 60 exposed at age 30**

Preliminary data – not for distribution

Breast Cancer

140 excess cases among 771



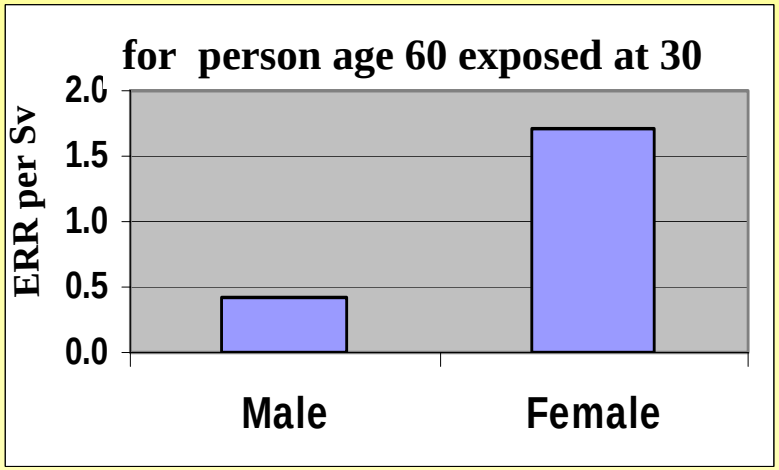
ERR/Sv = 0.46*

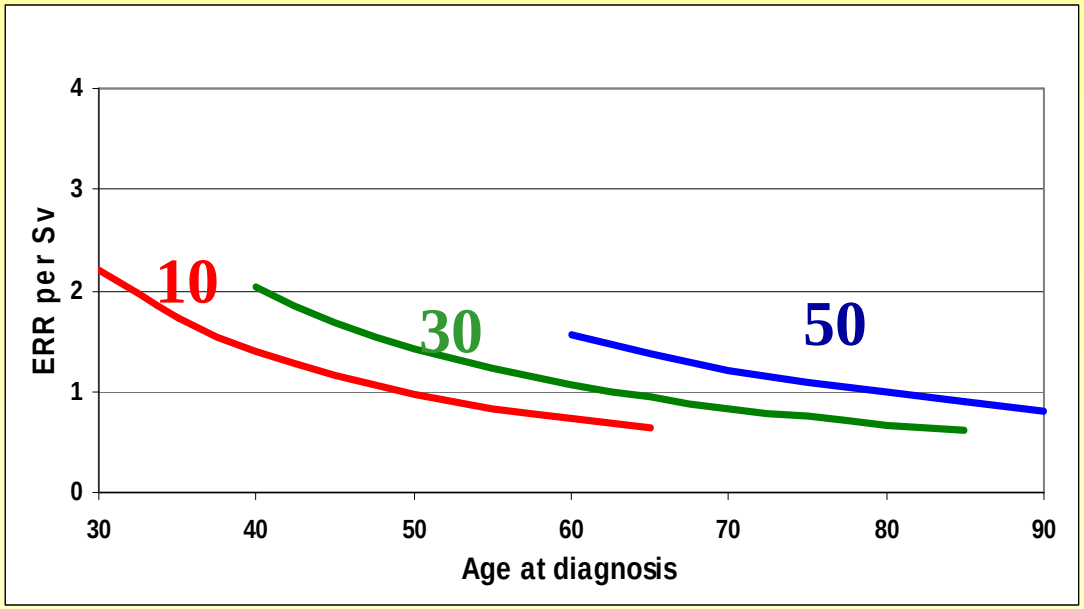
EAR/10^4 PYSv = 7.7*

***for person age 60 exposed at age 30**

Lung Cancer

107 excess cases





ERR/Sv* = 1.07

EAR/10^4 PY Sv* = 4.3

***for person age 60 exposed at age 30**

Site-Specific Incidence: Special Pathology Studies

- Additional case-finding
- Benign tumors
- Review of pathology slides and records
- Detailed histologic diagnosis
- Allow for additional analyses

Salivary Gland Tumors, 1950-87

Malignant (n=41)		Benign (n=94)	
ERR_{1Sv}	EAR/10^4 PY Sv	ERR_{1Sv}	EAR/10^4PYSv
3.5 (1.5-7.5)	3.7 (2.0-6.0)	0.7 (0.1-1.7)	1.9 (0.27-4.2)

Includes NIC, 90% CI; Land et al, 1996

Salivary Gland Tumors, 1950-87

	Malignant	Benign
No.	41	94
ERR_{1Sv}	3.5	0.7
	(1.5-7.5)	(0.1-1.7)
$EAR/10^4$ PY	3.7	1.9
	(2.0-6.0)	(0.27-4.2)

Includes NIC, 90% CI; Land et al, 1996

Salivary Gland Tumors, 1950-87

Level of risk differs by cell type

Mucoepidermoid carcinoma ERR_{Sv}=8.3
Other malignant ERR_{Sv}= 1.4

Warthin's tumor ERR_{Sv}= 3.1
Other benign ERR_{Sv}=0.3

Includes NIC, 90% CI; Land et al, 1996

Skin Tumors, 1958-89

Histology	ERR_{Sv}	90% CI
Melanoma	**2.1**	**<0.1; 12**
Nonmelanoma	**0.6**	**0.23; 1.3**
Basal cell	***1.8***	***0.83; 3.3***
Squamous cell	***<-0.1***	***<-0.1; 0.1***
Other epithelial	***1.4***	***0.02; 5.8***
Non-epithelial & NOS	***0.5***	***<-0.1; 6.7***
Bowen's tumor	**0.9**	**-0.4; 3.1**

Ron et al, 1998

Basal Cell Carcinoma, 1958-89

Age at Exposure	No. Cancers	ERR_{Sv} (90%CI)
0-9	3	21 (4.1 ; 73)
10-19	8	6.7 (2.1 ; 17)
20-39	28	1.7 (0.5 ; 3.8)
40+	41	0.7 (-0.05 ; 2.2)

Heterogeneity P=0.03; Trend P < 0.001

Ron et al, 1998

Basal Cell Carcinoma, 1958-89

UV exposure*	Cancers	ERR_{Sv} (90%CI)
High	37	0.4 (< -0.1 ; 2.1)
Low	43	4.7 (1.2 ; 13)

Heterogeneity P < 0.02

*Estimates for a person exposed to the bombings at age 30
High = face and hands; Low = rest of body

Skin Tumors

- Possible non-linear dose response
- Risk only for basal cell carcinoma
- Increased risk during childhood
- No interaction with UV
- Almost no melanomas

Nervous System Tumors, 1958-95

Histology	Cases	ERR_{Sv}	90% CI
All CNS	**228**	**1.2**	**0.7; 1.9**
Glioma	*43*	*0.56*	*-0.1; 1.8*
Meningioma	*88*	*0.64*	*0.03; 1.6*
Schwannoma	*55*	*4.5*	*2.0; 7.3*
Other	*42*	*0.51*	*-0.2-1.9*
Benign Pituitary	**35**	**0.98**	**-0.1; 3.1**

Preston et al, 2002

Preliminary data – not for distribution

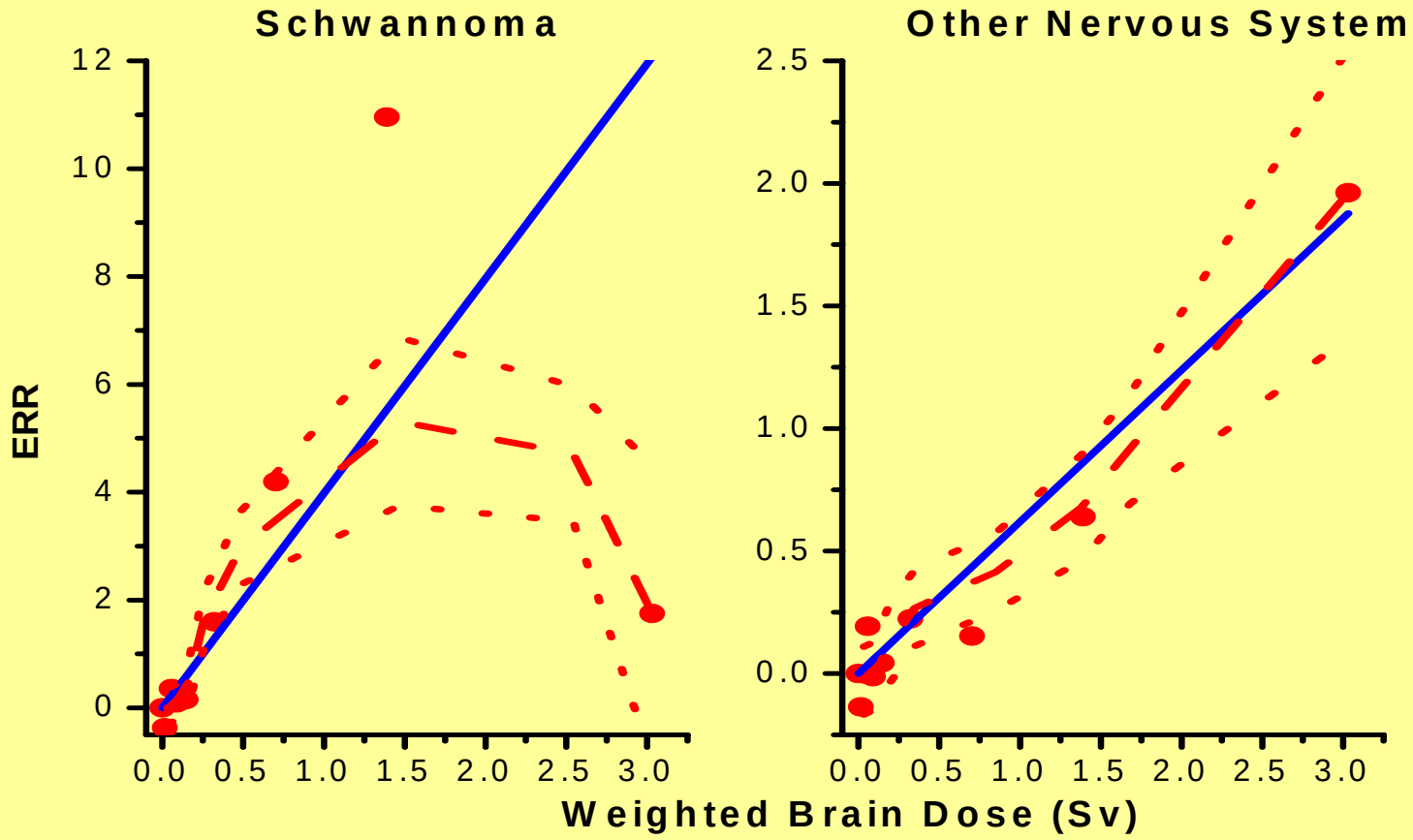
Nervous System Tumors, 1958-95

	Schwannoma	Other
Gender		
Male	8.0*	1.4
Female	2.4	0.11
	P= 0.12	*P=0.05*
Age at Exposure		
<20	6.0	1.2
20-40	2.7	0.3
40+	3.3	0.1
	P-trend >0.5	*P-trend=0.06*

*ERR_{Sv}

Preston et al, 2002

Nervous System Tumors, 1958-95 Dose Response



Preliminary data – not for distribution

CNS Tumors

- First time excess risk of all neural tumors combined seen in A-bomb survivors
- Risk continued throughout follow-up
- Highest risk seen for Schwannomas
- Age at exposure effect mostly for meningiomas
- Patterns of risk similar to other studies

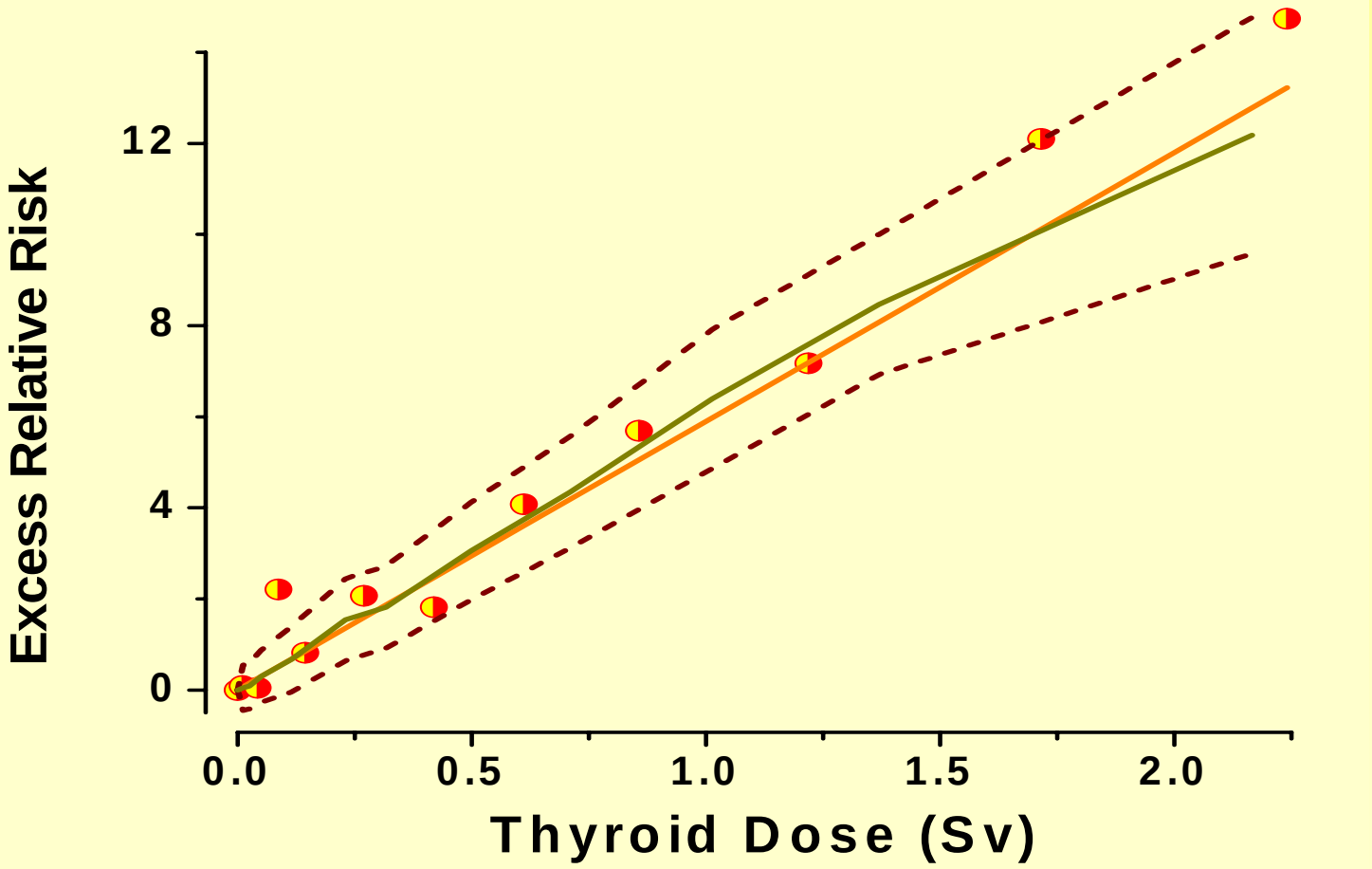
Thyroid Tumors, 1958-94

Tumors	Malignant	Benign
Non-autopsy	264 (84%)*	84 (82%)
Autopsy	133 (62%)	47 (68%)
Total	397 (77%)	131 (77%)

** (%) of cases in women*

Thyroid Cancer Dose Response

(for person age 0-9 at exposure)



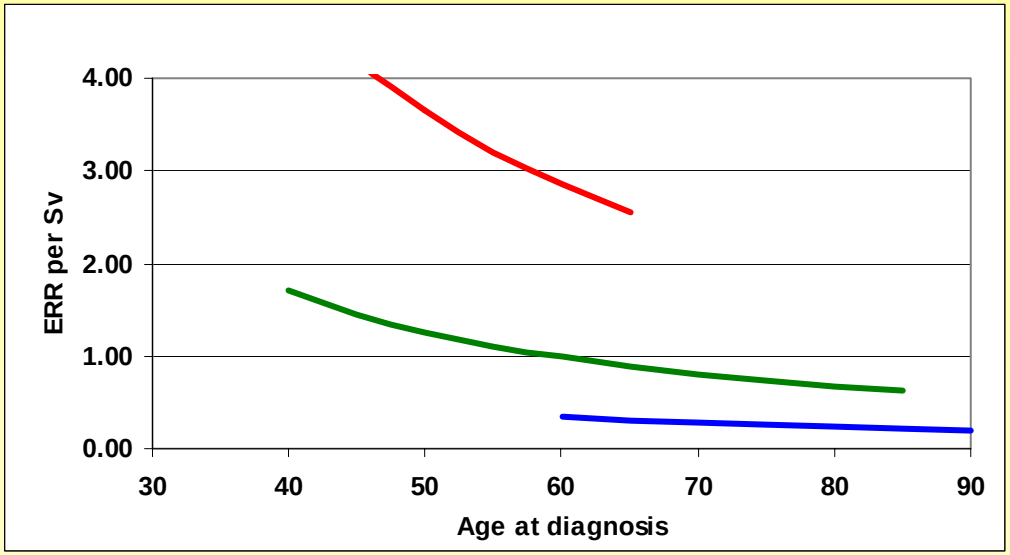
Preliminary data – not for distribution

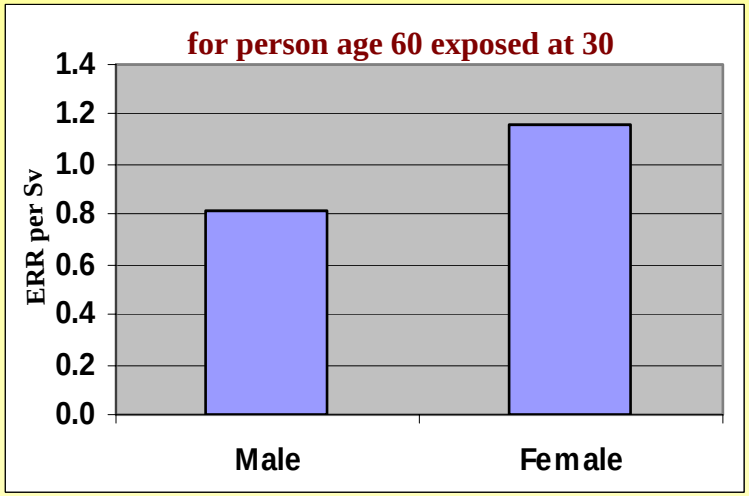
Thyroid Cancer, 1958-94

Age at exposure	Non-autopsy cases	All cases
0 – 9	6.3 (3.6; 10.2)*	6.6 (3.4; 12.4)
10 – 19	2.3 (1.1; 3.9)	2.1 (0.9; 4.0)
20 – 39	0.4 (-0.1; 3.9)	0.5 (0.0; 1.4)
40+	< 0 (-0.2; 0.6)	0.3 (-0.1; 1.0)

**Excess Relative Risks/Sv; 90% confidence interval*

Thyroid Cancer Incidence





ERR/Sv* = 0.99

EAR/10^4 PY Sv* = 1.2

71 excess cases

for person age 60 exposed at age 30

Age at Exposure

10 —— 30 —— 50 ——

Preliminary data – not for distribution

Benign Thyroid Tumors

Age at Exposure	Benign Tumors	ERR/Sv
0-9	24	2.5
10-19	29	<0
20-39	28	<0
40+	50	1.1

Thyroid Tumors

- Strong dose-response relation for thyroid cancers and benign tumors
- Risks decreased with increasing age at exposure
- Little evidence that high risks following childhood exposures decrease with time
- Patterns generally similar to those seen in other studies

NEW FINDINGS

- **Large excess relative risk for endometrial cancer among women exposed to the bomb before age 20**
- **Radiation effect observed for male breast cancer**

Summary (1)

- Solid cancer dose response continues to be linear
- Lifetime solid cancer excess estimated as about 10 times that for leukemia
- Excess risk continues throughout life

Summary (2)

- Age-time patterns don't differ substantially for most individual sites
- With more detailed analyses, age at exposure and attained age differences difficult to distinguish

Future

- **Continued follow-up is necessary to understand risk patterns for persons less than age 20 years ATB**

- **Additional site-specific incidence studies will provide needed information on the radiation-sensitivity of specific histologies**